REVIEW ARTICLE

A case report of obstetrical management of a pregnancy with hypermobile Ehlers–Danlos syndrome and literature review

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Summary: We present a case report of a successful pregnancy outcome in a woman diagnosed with Ehlers–Danlos syndrome (EDS) hypermobility type or type III. EDS is a group of connective tissue disorders that has a common genotypic defect, but heterogeneous phenotypic presentations. The variation in EDS manifestations can result in moderate to severe effects on life-expectancy for some types. A number of studies and a review of the literature indicate that generally in pregnant women with EDS, maternal and neonatal outcomes are favourable. However, in EDS type IV, pregnancy can be associated with serious maternal complications. Therefore, obstetrical management should be individualized. This paper discusses the obstetric management of a patient with EDS hypermobility type and compares it to other studies in the literature.

Keyword: Ehlers-Danlos syndrome

BACKGROUND

The earliest description of Ehlers–Danlos syndrome (EDS) was in the fourth century BC. In 1892, Tschernogobow wrote the first detailed clinical description of the syndrome. Reports by Edward Ehlers, a Danish dermatologist (1901), and Henri-Alexandre Danlos, a French physician (1908), led to the name of this condition.[1]

EDS is a group of connective tissue disorders that are divided into various distinguishable phenotypes. Common features include a decrease in tensile strength and integrity of the skin, hypermobility in the joints and other connective tissues, as well as skin hyperextensibility, tissue fragility, poor wound healing and easy bruising.[2]

EDS is an uncommon inherited disorder of collagen synthesis and the modes of inheritance vary significantly (autosomal dominant, autosomal recessive and X-linked inheritance patterns). Around 29 genes, which are located on chromosomes 15 and 24, contribute to the collagen protein structure and form at least 19 identifiable forms of collagen molecules, which normally provide strength and structure to skin, bone, blood vessels and internal organs.[3] A variety of gene mutations elicit collagen defects. There are six major types and at least five minor types of EDS.[4]

The major types include classic, hypermobility, vascular, kyphoscoliosis, arthrochalasia and dermatosparaxis. Some patients are difficult to categorize into one class only. The obstetrical complications relating to EDS are variable and infrequent, mainly depending on the type and severity of the disease. Some types are associated with severe maternal complications, whereas others are associated with more favourable outcomes.[5]

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CASE REPORT

A 34-year-old primigravida was booked for her antenatal care; she had a history of EDS. Due to the non-availability of a specific EDS-type genetic report, she was referred to a geneticist at around 20 weeks of gestation, who confirmed it was EDS hypermobility type. At 28 weeks, a cardiology review was organized and 12-lead echocardiogram (ECG) was within normal limits and echocardiography demonstrated that her aortic root was well within normal limits, measuring 2.8 cm. Cardiologists recommended a repeat ECG at 34 weeks, which was also within normal limits. She was seen by an obstetric anaesthetist and advised against epidural analgesia in view of the bruising tendency in EDS patients. She continued to receive care from both the cardiac and obstetric teams throughout her pregnancy.

The fetal growth scans at 28 and 34 weeks were normal. Her antenatal care was uneventful and she was induced at 40 weeks after spontaneous rupture of membranes. She received prostaglandin vaginally, as per the protocol of our department, and later started syntocinon infusion to augment labour. A healthy baby was delivered by emergency caesarean section, which was performed due to failure of progressing into the first stage. She received spinal analgesia for the caesarean section. There was no complication during the caesarean section and the patient made an unremarkable recovery. Our patient received entonox, pethidine and intravenous paracetamol for pain relief as the obstetric anaesthetist consultant advised against the use of epidural analgesia.

DISCUSSION

Abnormal collagen leads to the symptoms associated with EDS. The Classical type (formally types I and II) is linked to skin and soft tissue fragility, haemorrhage and poor wound healing. Some types are associated with more serious risks, e.g. vascular-type EDS can include rupture of internal organs

Table 1 **Obstetrical outcome of case reports of EDS hypermobility type**

	Sorokin *et al.*	Sakala *et al.*	Atalla *et al.*	Rochelson *et al.*	Morales *et al.*	Dutta *et al.*	Total (%)
Number of pregnancies	33	3	1	1	1	1	40
Term delivery	22	2	0	1	1	0	26 (65%)
PTL/PPROM	4	0	1	0	1	1	7 (17%)
Vaginal Delivery	26	2	0	1	1	0	30 (73%)
Caesarean Section	1	0	1	0	0	1	03 (7.5%)
Labour dystocia	3	0	0	0	0	0	03 (7.5%)
IUGR	2	0	0	0	0	0	02 (4.8%)
Live births	27	2	1	1	1	1	33 (82.5%)
Still births	0	0	0	0	0	0	0 (0%)
1st trimester Miscarriage	6	0	0	0	0	0	0 (14%)
2nd Trimester Miscarriages	1	1	0	0	0	0	02 (4.8%)
APH	4	0	0	0	0	1	05 (12%)
PPH	1	0	0	0	0	0	01 (2.4%)

PTL = preterm labour; PPROM = preterm prelabour rupture of membranes; IUGR = intrauterine growth restriction; APH = antepartum haemorrhage; PPH = postpartum haemorrhage)

or abnormal heart valves. The hypermobility type, formally known as type III, is characterized by the presence of a generalized joint laxity. Moreover, minimal vascular and skin involvement has been reported with good obstetrical outcome.[6]

The incidence of all types of EDS in pregnancy is estimated at 1 in 5000 to 1 in 20,000.[6] The classical EDS type represents 30% of the incidences, while EDS hypermobility type corresponds to around 35% and vascular EDS 10–30%. EDS does not reduce life-expectancy and pregnancy outcomes are similar to those in the general population, except for type IV, which carries a high risk of maternal morbidity and mortality that is estimated to be around 25%,[7] predominantly due to spontaneous arterial rupture.[8]

Ideally, EDS patients should receive prepregnancy counselling and the type and severity of EDS should be identified because it is a key factor in assessing potential obstetrical complications that may occur during pregnancy. The prepregnancy counselling helps to build a general outline of EDS-related obstetrical management options. In the most common types of EDS, pregnancy is not advised against, but involvement of a geneticist may help the patient to understand the inheritance pattern of their EDS case.[3] EDS hypermobility type is associated with relatively benign musculoskeletal problems, including joint dislocation and pain. There is debate in the literature about whether it is associated with prelabour rupture of membrane, preterm labour and failure to progress in labour. However, the data published so far do not support this association.[9]

The picture will become a little clearer if we compare the obstetric outcomes in EDS hypermobility type. One such comparison of published cases from developed countries has revealed that in spite of different managements, there is a good outcome in the majority of cases, which is evident in Table 1.

From this table it seems that the incidences of miscarriage, preterm birth, antepartum haemorrhage, labour dystocia, postpartum haemorrhage, vaginal deliveries and caesarean sections are not different from those in the general obstetrical population. The authors of various case reports, including Sorokin *et al.*[10], who presented the largest cases series of obstetrical outcome in EDS hypermobility type patients, concluded that this syndrome can result in uneventful pregnancies without an increase in musculoskeletal pain and joint dislocation, leading to successful vaginal deliveries. It is debatable whether hip or another pelvic joint dislocation is an indication for elective caesarean section, as mentioned in one case report. In other cases, vaginal birth was achieved with pelvic and hip dislocation problems.

In our case, the cardiologist reviewed the patient twice because EDS hypermobility type is known to have mild cardiovascular implications, i.e. tachycardia and chest pain. Aortic root dilation, usually of a mild degree, occurs in one-quarter to one-third of individuals with EDS classic and hypermobility types. There is no increased risk of aortic dissection in the absence of significant dilation. The long-term stability or progression and ultimate prognosis are not yet known.[11] There is no reported contraindication to any type of regional analgesia in EDS hypermobility type,[12] but in our case, epidural anaesthesia was advised against. However, there are reports of successful epidural combined with spinal analgesia in EDS hypermobility type pregnant patients and our patient tolerated spinal anaesthesia without complications. This highlights the importance of developing a consensus of opinion regarding the specific management of EDS patients.

CONCLUSION

It is evident from a review of the literature that due to the uncommon nature of EDS hypermobility type, and in the absence of obstetric management guidelines for EDS pregnancies, such cases have to be managed on an individual basis. It seems that well-supervised EDS hypermobility type pregnancies are not associated with additional maternal or fetal complications, and that the majority results in healthy outcomes. It is appropriate to suggest that pregnant women with EDS hypermobility type can be managed through multidisciplinary input, but mostly will not require additional intervention compared with their low risk obstetrical counterparts.

DECLARATIONS

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